REMARKS

Claims 1-41 are pending with claims 18, 19, 21, 22, 27, and 31-41 under examination. Applicants have amended claim 21 to recite the full name for the acronym "SVZ." The specification supports this amendment at page 21, lines 21-23. Applicants also amended claims 27 and 34 to describe the recited "C-S mutant Galectin-1." This amendment is supported at page 6, lines 19-23. New claims 38-41 are supported by the specification at, for example, page 10, lines 16-18. Applicants contend that these claim amendments do not add new matter.

The Office rejects claims 18, 19, 21, 22, 27, and 31-37 under 35 U.S.C. §103(a). As a preliminary matter, Applicants address the Office's objections to the specification and to the claims.

Objections to the Specification

The Office objects to the specification at page 3 because of the apparent misspelling of the term "Galectin." Applicants have amended the specification at page 3 to correct the spelling of this term as requested by the Office. Applicants therefore request that the Office withdraw this objection.

The Office objects to the last paragraph on page 15 of the specification, because the usage of the term "each" is unclear. Applicants have amended this paragraph to clarify the use of this term. Applicants request that the Office withdraw this objection.

The Office objects to the sentence at page 22, lines 24-25 of the specification because this sentence is allegedly grammatically incorrect. Applicants respectfully contend that this sentence is clear as written. The sentence, which spans lines 24-27, describes four functions of some SVZ astrocytes. Specifically, the sentence instructs that a "part of SVZ astrocytes *function* as stem cells, *differentiate* into transit amplifying

cells (TA cells) at the mid-stage of differentiation, *proliferate* again, and *differentiate* into neuroblasts (NBs)." Emphasis added. Because the sentence is clear as written, Applicants request that the Office withdraw this objection.

Objections to the Claims

The Office objects to claims 21, 27, 34, and 36 for recitation of the terms "SVZ" and "C-S," believing that these terms are abbreviations. With regard to the term "SVZ," Applicants amended claim 21 to recite the full name for this term. The term "C-S" is not an abbreviation, but rather part of a specific term ("C-S mutant Galectin-1") defined in the specification. As the specification explains,

> a "C-S mutant Galectin" refers to a mutant Galectin-1 protein in which at least one cysteine residue among the cysteine residues possessed by Galectin is mutated to a serine residue.

Specification at page 6, lines 19-23. Solely to facilitate prosecution, Applicants amended claims 27 and 34 to make explicit what was already implicit in these claims by incorporating the specification's definition of the term "C-S mutant Galectin-1" into these claims. Applicants request that the Office withdraw this objection.

Rejections Under 35 U.S.C. §103(a)

Claims 18, 19, 27, and 31-35 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent 6,890,531 ("Horie") in view of Wells et al. (*Cell* 64:91-97 (1991); "Wells"). According to the Office, Horie teaches a method for treating divergent neurological disorders including neurodegenerative diseases such as neuropathy and nerve injury resulting from ischemia. Horie also allegedly discloses treatment of nerve damage resulting from central and peripheral nerve injuries comprising treatment of degenerating nerve tissue and promoting regeneration of

neurites. While Horie does not explicitly teach administration of Galectin-1 to the brain, the Office reasons that Horie's alleged teaching of administering Galectin-1 to the site of injury "implicitly requires administration to the brain as the nerve tissue." Office Action, p. 5. Because Horie does not teach that Galectin-1 is involved in cell proliferation, the Office turns to Wells for allegedly disclosing "a β galactoside binding animal lectin, i.e., Galactin-1, which is expressed constitutively and operates in regulation of cell proliferation."

Based on the alleged teachings in Horie and Wells, the Office reasons that one of ordinary skill in the art would recognize that treatment of cerebral ischemia and neural degenerative disease by administration of Galectin-1 implicitly involves regeneration and remyelinization from nerve injuries as well as regulation of cell proliferation. Admitting that neither Horie nor Wells teach the proliferation of neuronal stem cells, the Office nonetheless contends that "proliferation of neural stem cells . . . would be intrinsically necessary to the administration of Galactin-1 as Galactin-1 regulates constitutively cell division." Office Action, p. 6. The Office believes that one of ordinary skill in the art would have had a reasonable expectation of success "given the results of both publications demonstrating the success of the methodology." *Id.* Applicants traverse.

As an initial matter, Applicants contend that the Office's basis for a reasonable expectation of success is inadequate. As the Supreme Court has instructed,

> [t]o facilitate review [of an obviousness rejection], this analysis should be made explicit. . . . Rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.

KSR Intern. Co. v. Teleflex Inc., 127 S.Ct. 1727, 1741 (2007). In the Office Action, the Office summarizes what it believes are the teachings of Horie and Wells and then concludes that there would have been a reasonable expectation of success based on a general statement about the "results of both publications." Notably, the Office provides the same kind of general reasoning to support its conclusion of obviousness based on the combination of Horie, Wells, Gage, and Taupin, discussed below. Applicants respectfully contend that the Office should provide the required analysis by pointing to specific results in each reference and explaining why it believes those results support a conclusion of obviousness. Notwithstanding the Office's lack of a *prima facie* case of obviousness, Applicants address the Office's comments in the interests of expediting prosecution.

As noted above, the Office admits that neither Horie nor Wells teach the proliferation of neuronal stem cells. Despite this admission, the Office still contends that proliferation of neural stem cells . . . would be intrinsically necessary to the administration of Galactin-1 because Galactin-1 regulates constitutively cell division. Applicants disagree with the Office's assumption. Horie identified Galectin-1 as a nerve regeneration-promoting factor (see col. 4, lines 37-46). Moreover, the only experiments disclosed in Horie that addressed effects on nerve injury or nerve regeneration were carried out on the sciatic nerve (Example 18) or on a transected fibular portion of the sciatic nerve (Example 19), respectively. Applicants contend that there is no teaching in Horie that neural stem cells are associated with the sciatic nerve. Indeed, the phenomenon of nerve regeneration in a peripheral nerve such as the sciatic nerve is completely different from the proliferation of a neural stem cell.

Adding Wells does not compensate for the lack of teaching in Horie. First, Wells does not disclose any experiments on nerve cells, let alone neural stem cells. Rather, Wells performs experiments on fibroblasts. Moreover, Wells teaches that murine β-galactoside-binding protein (mGBP) is a *negative* regulator of cell proliferation. See, e.g., p. 94, left col., lines 4-6 and p. 95, left col., first paragraph, lines 3-5. There is no teaching or suggestion in Wells that Galectin-1 can enhance cell proliferation and if anything teaches away from the claimed invention. Thus, the combination of Horie and Wells would not have rendered claims 18, 19, 27, and 31-35 obvious. Applicants therefore request that the Office withdraw this rejection.

The Office rejects claims 21, 22, 36, and 37 under 35 U.S.C. §103(a) as allegedly obvious over Horie in view of Wells and in further view of U.S. Patent 6,436,389 ("Gage") or Taupin et al. (*Neuron* 28:385-97 (2000); "Taupin"). The Office applies Horie and Wells as described above. Acknowledging that neither of these references teach the subventricular region of the brain, the Office turns to Gage for allegedly teaching treatment of neurodegenerative diseases comprising injecting modified adult hippocampus-derived neuronal progenitor cells (AHPs) into the rat hippocampus. Gage also allegedly uses glial fibrillary acidic protein to detect *in vivo* proliferation of embryonic rat primary hippocampal neural progenitor cells and teaches that intracerebral administration of FGF-2 has been shown to stimulate neurogenesis in the adult rat subventricular region of the brain. The Office contends that Taupin also teaches cell division in the neurogenic regions of the rat subventricular region after injection of genetically modified AHPs into the rat hippocampus.

Combining these references, the Office concludes that one of ordinary skill in the art would recognize that treatment of cerebral ischemia and neural degenerative disease by administration of Galectin-1 implicitly involves regeneration and remyelinization from nerve injuries as well as regulation of cell proliferation. Admitting that neither Horie, Wells, Gage, nor Taupin teach the proliferation of neuronal stem cells, the Office nonetheless contends that "proliferation of neural stem cells . . . would be intrinsically necessary to the administration of Galactin-1 as Galactin-1 regulates constitutively cell division." Office Action, p. 8. According to the Office, it would have been *prima facie* obvious for one of ordinary skill in the art, as a matter of design choice, to administer Galectin-1 to any brain region associated with the contemplated treatment of neurological disorders in order to ameliorate said disorder because neurodegenerative diseases result from alterations of physiological regulation in nerve brain cells. The Office believes that one of ordinary skill in the art would have had a reasonable expectation of success to use the methods of enhancing cell proliferation by administering Galectin-1 for the treatment of cerebral ischemia as allegedly taught by Horie, Wells, Gage, and Taupin "given the results of the publications demonstrating the success of the methodology." *Id.* Applicants traverse.

As Applicants explained and the Office admits, neither Horie nor Wells teach the enhancement of *in vivo* proliferation of a neural stem cell by administering Galectin-1. If anything, Wells teaches away from this concept. As with Horie and Wells, the Office also admits that neither Gage nor Taupin teach this concept either. Indeed, Gage and Taupin do not even mention Galectin-1 and therefore cannot remedy the shortcomings of Horie and Wells as discussed above. Thus, for the reason stated above, the

combination of Horie, Well, Gage, and Taupin would not have rendered the invention of claims 21, 22, 36, and 37 obvious. Applicants request that this rejection be withdrawn.

Conclusions

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of claims 18, 19, 21, 22, 27, and 31-41.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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